Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	427	thymosin same interfer$	USPAT; EPO; DERWENT	OR	OFF	2005/01/10 14:21
L2	347	1 and combinat$	USPAT; EPO; DERWENT	OR	OFF	2005/01/10 14:21
L3	34	1 and (combinat$ near5 (therap composition))	USPAT; EPO; DERWENT	OR	OFF	2005/01/10 14:21
L4	116	1 and (combinat$ near5 (therap$ composition))	USPAT; EPO; DERWENT	OR	OFF	2005/01/10 14:23
L5	99	1 and (combinat$ near5 (therap$))	USPAT; EPO; DERWENT	OR	OFF	2005/01/10 14:26
L6	53	thymosin$ near7 interferon	USPAT; EPO; DERWENT	OR	OFF	2005/01/10 14:26

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12/7/25
DIALOG(R)File 155:MEDLINE(R)

10281246 PMID: 7526795
Prospectives on the treatment of chronic hepatitis B and chronic hepatitis C with thymic peptides and antiviral agents.
Mutchnick M G; Ehrinpreis M N; Kinzie J L; Peleman R R
Department of Medicine, Wayne State University School of Medicine, Detroit, MI 48201.
Antiviral research (NETHERLANDS) Jul 1994, 24 (2-3) p245-57, ISSN 0166-3542 Journal Code: 8109699
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
At the present time, interferon is considered the only effective therapeutic approach in the treatment of both chronic hepatitis B and chronic hepatitis C. It is clear that the disappointing response rates in both chronic hepatitis B and C place added emphasis on efforts to identify alternative forms of therapy. In addition to the development of other antiviral agents including the nucleoside analogs which might prove more effective and have fewer associated side-effects, other agents currently under investigation include thymic peptides such as thymosin alpha 1. In the future, the therapeutic approach to the treatment of chronic hepatitis B and C may consist of combination therapy using perhaps an immune modulator and an antiviral agent or, several antiviral drugs. Alternatively, there is indication that cellular targeting systems with delivery of the toxic material to the specific cell containing the virus may be more effective, while minimizing side-effects. Finally, there are agents such as ursodeoxycholic acid which perhaps, makes bile less toxic and can be used as adjunctive therapy with improvement in liver chemistry values. The treatment of chronic hepatitis B and chronic hepatitis C has shifted in emphasis form the concept of treating liver disease towards that of treating viral infections which happen to effect primarily the liver. (65 Refs.)
Record Date Created: 19941207
Record Date Completed: 19941207

12/7/26
DIALOG(R)File 155:MEDLINE(R)

10146058 PMID: 8038356
Rolling review--the pathogenesis, diagnosis and management of viral hepatitis.
Dusheiko G M
Royal Free Hospital and School of Medicine, London, UK.
Alimentary pharmacology & therapeutics (ENGLAND) Apr 1994, 8 (2) p229-53, ISSN 0269-2813 Journal Code: 8707234
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Five major hepatotrophic viruses have been identified. The pathogenesis, diagnosis and treatment of chronic viral hepatitis continues to be intensely researched. Experimental evidence suggests that HLA restricted virus-specific T cells play a role in hepatocellular injury in type A

hepatitis. The absence of chronic infection indicates the effectiveness of the host immune response to hepatitis A virus (HAV). It is postulated that HAV may rarely trigger an autoimmune chronic hepatitis. Active prophylaxis of hepatitis A is possible. The elimination of hepatitis B is dependent on the recognition of viral determinants in association with HLA proteins on infected hepatocytes by cytotoxic T cells. The specific epitopes recognized by B and T cells are being mapped. Polymerase chain reaction (PCR) amplification and sequencing of genomic DNA in patients with chronic hepatitis B has indicated that nucleotide substitutions in the genome are not uncommon. Their pathogenicity is being explored. Antiviral therapy for hepatitis B remains difficult. Interferon is effective in a proportion of patients. Thymosin may prove to be more effective immunomodulatory therapy. New nucleoside analogues suppress HBV replication, but the safety of these drugs has been questioned after the appearance of severe liver toxicity with fialuridine. The data that hepatitis D virus is pathogenic has recently been challenged with the observation that HDV re-occurs in transplanted liver after engrafting, but without signs of HBV recurrence or evidence of liver damage. Treatment of hepatitis D virus remains difficult. Several isolates of hepatitis C virus have been cloned, and the sequence divergence of these isolates indicates that there are several major genotypes and component subtypes of this polymorphic virus.(ABSTRACT TRUNCATED AT 250 WORDS) (161 Refs.)

Record Date Created: 19940825

Record Date Completed: 19940825

12/7/27

DIALOG(R)File 155:MEDLINE(R)

09986540 PMID: 8109588

New approaches to the treatment of chronic viral hepatitis B and C.

Regenstein F

Ochsner Medical Institutions, New Orleans, Louisiana 70121.

American journal of medicine (UNITED STATES) Jan 17 1994, 96 (1A) p47S-51S, ISSN 0002-9343 Journal Code: 0267200

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Interferon treatment of hepatitis B and C virus (HBV, HCV) infections has been hampered by overall initial response rates of < 50%, a relapse rate that is > 50% for patients with chronic HCV, and rare responses in individuals with chronic HBV who are immunosuppressed or immunologically tolerant to the HBV. Because of these difficulties, the efficacy of other therapeutic agents is being vigorously explored. Among the immunomodulatory agents being evaluated, thymosin appears to be a promising new therapy for HBV. Results from an ongoing multicenter trial evaluating thymosin are expected next year. A variety of nucleoside analogues with antiviral activity against the HBV have also been identified. Several of the more active agents deserve further study in clinical trials. In chronic HCV infection, only interferon therapy has been extensively studied. Ribavirin alone may have some value, but its precise role in the treatment of chronic HCV will require additional testing. Interferon therapy for patients with chronic HBV or HCV infection represents an important first step in the treatment of these disorders. In the absence of an ideal antiviral agent, however, combinations of the available antiviral and immunomodulatory agents or synergistic combinations of antiviral agents need to be studied in order to achieve better therapeutic responses. (48 Refs.)

Record Date Created: 19940322

Record Date Completed: 19940322

12/7/28
DIALOG(R)File 155:MEDLINE(R)

09846612 PMID: 8407692
Treatment of chronic viral hepatitis.
Dusheiko G M; Zuckerman A J
University Department of Medicine, Royal Free Hospital and School of Medicine, London, UK.
Journal of antimicrobial chemotherapy (ENGLAND) Jul 1993, 32 Suppl A p107-20, ISSN 0305-7453 Journal Code: 7513617
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A substantial number of anti-viral compounds have been evaluated for the treatment of patients with chronic viral hepatitis. A few of these compounds have now achieved clinical applicability. alpha-Interferon is the most widely studied and remains the main treatment for chronic hepatitis B and C. Unfortunately in both these conditions only a minority of patients respond to interferon therapy, although the response can be complete in some patients. Some parameters have been identified which assist in the selection of patients for treatment. Several other cytokines, including thymosin, have been evaluated for the treatment of chronic hepatitis B. There are a number of promising new nucleosides which may inhibit hepatitis B virus and their action is being studied. Relapse rates are unknown however with these compounds. Ribavirin, a guanosine analogue, is also efficacious in treating a proportion of patients with chronic hepatitis C and the drug may be useful in treating patients with cirrhosis or patients who have an auto-immune diathesis. (88 Refs.)
Record Date Created: 19931108
Record Date Completed: 19931108

12/7/29
DIALOG(R)File 155:MEDLINE(R)

09441216 PMID: 1382288
Chronic hepatitis B and C. What is the status of drug therapy?
Wright T L
Division of Gastroenterology and Hepatology, School of Medicine, University of California, San Francisco.
Postgraduate medicine (UNITED STATES) Sep 15 1992, 92 (4) p75-82, ISSN 0032-5481 Journal Code: 0401147
Document type: Clinical Trial; Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Chronic hepatitis remains difficult to treat. Use of interferon has been successful against both hepatitis B and C viruses, but the outcome of long-term administration has yet to be determined. Not all patients respond to interferon, however, and some have side effects that cause them to discontinue therapy. Dr Wright discusses the results of studies to evaluate therapy with alpha, beta, and gamma interferon as well as with other agents, such as ribavirin, thymosin, and ursodeoxycholic acid. (32 Refs.)
Record Date Created: 19921022
Record Date Completed: 19921022
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12/7/1
DIALOG(R)File 155:MEDLINE(R)

17550064 PMID: 15546255
Combination therapy of thymalfasin (thymosin-alpha 1) and peginterferon alfa-2a in patients with chronic hepatitis C virus infection who are non-responders to standard treatment.
Rustgi Vinod
Liver Transplantation Unit, Georgetown University Medical Center, Washington, DC, USA.
Journal of gastroenterology and hepatology (Australia) Dec 2004, 19 Suppl 6 pS76-8, ISSN 0815-9319 Journal Code: 8607909
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Data Review
Abstract The worldwide spread of hepatitis C virus is enormous; chronic hepatitis C virus infection is a leading cause of liver cirrhosis and hepatocellular carcinoma. While treatment options have improved substantially over the last decade, responses are still disappointing, particularly in certain difficult-to-treat groups such as patients who are immunosuppressed or have decompensated disease. Preliminary studies have indicated that combined treatment strategies may provide effective approaches for the future. The combination of thymalfasin with pegylated interferon is currently a promising option for the treatment of patients with chronic hepatitis C virus infection. An ongoing phase 3 study in the USA should provide much needed data to improve the outcome for these patients. (c) 2004 Blackwell Publishing Asia Pty Ltd.
Record Date Created: 20041119

12/7/2
DIALOG(R)File 155:MEDLINE(R)

17133413 PMID: 15468612
Retreatment of patients who do not respond to initial therapy for chronic hepatitis C.
Shiffman Mitchell L
Hepatology Section, Virginia Commonwealth University Medical Center, Box 980341, Richmond, VA 23298, USA. mlshiffm@vcu.edu
Cleveland Clinic journal of medicine (United States) May 2004, 71 Suppl 3 pS13-6, ISSN 0891-1150 Journal Code: 8703441
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Despite improvements in the treatment of chronic hepatitis C virus (HCV) infection, nearly half of all patients do not respond to initial therapy. Retreatment of these patients with pegylated interferon and ribavirin has been successful in only a limited percentage of cases. Factors associated with sustained virologic response (SVR) following retreatment include prior treatment with interferon monotherapy, HCV genotype 2 or 3, a low serum HCV RNA level, and the absence of cirrhosis. Fewer than 6% of nonresponders who were previously treated with interferon and ribavirin and who have cirrhosis, genotype 1, and a high viral load achieve SVR following retreatment with pegylated interferon and ribavirin. No therapy has been

shown to yield SVR in patients who do not respond to pegylated interferon and ribavirin. Long-term maintenance therapy with pegylated interferon is currently being evaluated in nonresponders with advanced fibrosis and cirrhosis. Its use should be considered investigational at this time. (18 Refs.)
Record Date Created: 20041007
Record Date Completed: 20041025

12/7/3
DIALOG(R)File 155:MEDLINE(R)

16658603 PMID: 15081103
Future trends in managing hepatitis C.
McHutchison John G; Dev Anouk T
Division of Gastroenterology and GI/Hepatology Research, Duke Clinical Research Institute, Duke University Medical Center, P.O. Box 17969, Durham, NC 27710, USA. mchut001@mc.duke.edu
Gastroenterology clinics of North America (United States) Mar 2004, 33 (1 Suppl) pS51-61, ISSN 0889-8553 Journal Code: 8706257
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Despite recent improvements in the treatment of patients who have chronic hepatitis C, a large proportion of patients do not achieve viral clearance. Treatment regimens are also costly, associated with significant morbidity, require substantial patient commitment, and are not appropriate for all patients. Therefore, it is important to maximize and enhance current therapeutic approaches and to investigate new approaches and therapies. Because the ability to maintain adherence to current treatment is associated with higher sustained virologic response rates (particularly in patients infected with genotype 1), strategies directed at patients and support staff to promote treatment adherence are important. Other strategies to enhance current therapy include alternative interferons (IFNs)/cytokines and new IFN delivery systems. Current therapy may also be enhanced by new ribavirin (RBV) analogs with an improved safety profile or by the addition of other immunomodulatory agents such as inosine 5'-monophosphate dehydrogenase inhibitors, histamine dihydrochloride, thymosin alfa 1, and amantadine. Some of these agents have demonstrated promising results, although further evaluation is required. Greater knowledge of the molecular biology of the hepatitis C virus (HCV) holds promise for the development of targeted therapies such as specific inhibitors of HCV polymerase, protease, or helicase, as well as therapeutic vaccines. Other potential molecular-based therapies include antisense oligonucleotides, ribozymes, and short interfering ribonucleic acid (RNA) molecules. Therapies aimed at reducing or preventing the development of fibrosis are also under investigation. Multiple-drug regimens will likely be required to enhance viral clearance and reduce viral resistance, while providing greater tolerability.
Record Date Created: 20040414
Record Date Completed: 20040812

12/7/4
DIALOG(R)File 155:MEDLINE(R)

15904365 PMID: 14738560
Thymosin-alpha 1 plus interferon-alpha for naive patients with chronic hepatitis C: results of a randomized controlled pilot trial.

Andreone P; Gramenzi A; Cursaro C; Felline F; Loggi E; D'Errico A; Spinosa M; Lorenzini S; Biselli M; Bernardi M

Semeiotica Medica, Dipartimento di Medicina Interna, Cardioangiologia ed Epatologia, Universita di Bologna Istituto Oncologico, Italy. andreone@med.unibo.it

Journal of viral hepatitis (England) Jan 2004, 11 (1) p69-73, ISSN 1352-0504 Journal Code: 9435672

Document type: Clinical Trial; Journal Article; Multicenter Study; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

In this pilot study, we evaluated the efficacy of interferon-alpha (IFN) plus Thymosin-alpha 1 (TA1) to that of IFN alone in naive patients with chronic hepatitis C. Twenty-two patients were randomized to receive interferon-alpha 2b (3 million units three times a week) plus thymosin-alpha 1 (900 microg/m2 body surface area) and 19 received interferon-alpha 2b alone at the same dose. Patients were treated for 6 months and followed up for another 6 months. Biochemical (alanine aminotransferase values) and virological (hepatitis C virus-RNA) responses to treatment were determined. Combination treatment showed significantly higher efficacy than monotherapy in achieving virological end-of-treatment response (P = 0.03). At 6-month follow up, the sustained biochemical and virological response was not different between the two groups. Our results indicate that the immune modulator TA1 may enhance the end-of-treatment response in naive patients with chronic hepatitis C. Higher doses and/ore more prolonged courses as well as the association with new interferon formulation such as pegylated interferons could improve the sustained response rates to this treatment.

Record Date Created: 20040123

Record Date Completed: 20040330

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Set     Items   Description
S1        536   INTERFERON (S) THYMO?
S2        287   S1 NOT PY>1992
S3         34   S2 AND (COMBINAT? OR CO () ADMIN?)
S4        110   THYMOSIN (S) (IFN OR INTERFERON)
S5         36   S4 NOT PY>1991
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09/544,108

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